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=> File Medline EMBASE Biosis Caplus

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FILE 'MEDLINE' ENTERED AT 21:17:00 ON 10 AUG 2005

FILE 'EMBASE' ENTERED AT 21:17:00 ON 10 AUG 2005

FILE 'BIOSIS' ENTERED AT 21:17:00 ON 10 AUG 2005

FILE 'CAPLUS' ENTERED AT 21:17:00 ON 10 AUG 2005

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=> s (Asp2 or BACE) (10A) (protease or peptidase or proteinase)
L1 355 (ASP2 OR BACE) (10A) (PROTEASE OR PEPTIDASE OR PROTEINASE)

=> s (protease or peptidase or proteinase or cleavage or cleaved or cleave) (6A) (site or motif)
L2 72218 (PROTEASE OR PEPTIDASE OR PROTEINASE OR CLEAVAGE OR CLEAVED OR
CLEAVE) (6A) (SITE OR MOTIF)

=> s (Asp2 or BACE) (6A) (engineer or engineered or recombinant or (fusion (w) protein))
L3 44 (ASP2 OR BACE) (6A) (ENGINEER OR ENGINEERED OR RECOMBINANT OR
(FUSION (W) PROTEIN))

=> s l1 and l2 and l3
L4 6 L1 AND L2 AND L3

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L5 3 DUPLICATE REMOVE L4 (3 DUPLICATES REMOVED)

=> s EINLETD
L6 0 EINLETD

=> d l5 1-3 bib ab

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:588488 CAPLUS
DN 143:92074
TI Modified pro-β-secretase/BACE-1 and production of β-secretase/**BACE**-1 with **recombinant** cells
IN Ballinger, Marcus; Randal, Michael L.
PA Sunesis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005060384	A2	20050707	WO 2004-US21816	20040707

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005074456 A1 20050407 US 2003-726967 20031202
PRAI US 2003-726967 A 20031202
US 2002-430984P P 20021204

AB The present invention is directed to **engineered** polypeptides having **BACE** activity. In certain embodiments, the polypeptides also comprise an engineered **cleavage site**. Also provided are polypeptides comprising a prodomain, an engineered **cleavage site**, and a **protease** domain. The polypeptides are properly folded and are **cleaved** at the engineered **cleavage site** in vitro, producing homogeneous prepns. of purified **protease** having **BACE** activity. The invention further pertains to nucleic acids, expression vectors, and host cells comprising the expression vectors for making the engineered polypeptides.

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:247466 CAPLUS
DN 134:277406
TI Cloning and characterization of mammalian secretase isoenzymes, their amyloid precursor protein substrates, and uses for treatment or prevention of Alzheimer's disease
IN Gurney, Mark; Bienkowski, Michael Jerome
PA Pharmacia & Upjohn Company, USA
SO PCT Int. Appl., 189 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 8

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001023533	A2	20010405	WO 2000-US26080	20000922
WO 2001023533	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2000017369	A2	20000330	WO 1999-US20881	19990923
WO 2000017369	A3	20001123		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6699671	B1	20040302	US 1999-416901	19991013
CA 2397786	AA	20010405	CA 2000-2397786	20000922
AU 2000076071	A5	20010430	AU 2000-76071	20000922
EP 1224297	A2	20020724	EP 2000-965338	20000922

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL
NZ 517297 A 20040430 NZ 2000-517297 20000922
PRAI US 1999-155493P P 19990923
US 1999-404133 A 19990923
WO 1999-US20881 A2 19990923
US 1999-416901 A2 19991013
US 1999-169232P P 19991206
US 1998-101594P P 19980924
WO 2000-US26080 W 20000922
AB The present invention provides the enzyme and enzymic procedures for
cleaving the β secretase **cleavage site** of the
amyloid precursor (APP) protein and associated nucleic acids, peptides,
vectors, cells and isolates and assays. The identification and
characterization of the β secretase enzyme, termed Aspartyl
Protease 2 (**Asp2**) is disclosed. The authors also
identify and characterize both α-secretase and β-secretase
activities of a protease, designated as Asp1. Amino acid and encoding
cDNA sequences of human Asp1, and two alternative splice variants of the
secretase Asp2, human and murine Asp2(a) and Asp2(b), are provided. The
authors describe regions in the proteases critical for their unique function
and for the first time characterize their substrate. This is the first
description of expressed isolated purified active protein of this type,
assays that use the protein, in addition to the identification and creation
of useful cell lines and inhibitors. The Asp1 processes the APP protein
at the α-secretase site. The invention further provides a modified
APP protein and associated nucleic acids, peptides, vectors, cells, and cell
isolates, and assays that are particularly useful for identifying
candidate therapeutics for treatment or prevention of Alzheimer's disease.

L5 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1
AN 2001078285 MEDLINE
DN PubMed ID: 10956649
TI A furin-like convertase mediates propeptide cleavage of BACE, the
Alzheimer's beta -secretase.
CM Erratum in: J Biol Chem 2001 May 4;276(18):15561
AU Bennett B D; Denis P; Haniu M; Teplow D B; Kahn S; Louis J C; Citron M;

Vassar R
CS Department of Neurology, Harvard Medical School, and Center for Neurologic
Diseases, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.
SO Journal of biological chemistry, (2000 Dec 1) 275 (48) 37712-7.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010723
Entered Medline: 20010111
AB The novel transmembrane aspartic **protease BACE** (for Beta-**site** APP Cleaving Enzyme) is the beta-secretase that cleaves amyloid precursor protein to initiate beta-amyloid formation. As such, BACE is a prime therapeutic target for the treatment of Alzheimer's disease. **BACE**, like other aspartic **proteases**, has a propeptide domain that is removed to form the mature enzyme. BACE propeptide cleavage occurs at the sequence RLPR downward arrowE, a potential furin recognition motif. Here, we explore the role of furin in BACE propeptide domain processing. BACE propeptide cleavage in cells does not appear to be autocatalytic, since an inactive D93A mutant of BACE is still cleaved appropriately. BACE and furin co-localize within the Golgi apparatus, and propeptide cleavage is inhibited by brefeldin A and monensin, drugs that disrupt trafficking through the Golgi. Treatment of cells with the calcium ionophore, leading to inhibition of calcium-dependent proteases including furin, or transfection with the alpha(1)-antitrypsin variant alpha(1)-PDX, a potent furin inhibitor, dramatically reduces cleavage of the BACE propeptide. Moreover, the BACE propeptide is not processed in the furin-deficient LoVo cell line; however, processing is restored upon furin transfection. Finally, in vitro digestion of **recombinant** soluble **BACE** with **recombinant** furin results in complete **cleavage** only at the established E46 **site**. Taken together, our results strongly

suggest that furin, or a furin-like proprotein convertase, is responsible for cleaving the BACE propeptide domain to form the mature enzyme.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	51	(Asp2 or BACE) and (protease or peptidase or proteinase)	USPAT	OR	OFF	2005/08/10 20:56
L2	15650	(protease or peptidase or proteinase or cleavage or cleaved or cleave) near6 (site or motif)	USPAT	OR	OFF	2005/08/10 20:56
L3	34	l1 and l2	USPAT	OR	OFF	2005/08/10 20:56
L4	43	(Asp2 or BACE) near6 (engineer or engineered or recombinant or (fusion (w) protein))	USPAT	OR	OFF	2005/08/10 20:57
L5	28	l3 and l4	USPAT	OR	OFF	2005/08/10 21:11
L6	0	EINLETD	USPAT	OR	OFF	2005/08/10 21:11